



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,329	01/25/2002	Tasuku Honjo	Q61531	7110

23373 7590 08/18/2003

SUGHRUE MION, PLLC  
2100 PENNSYLVANIA AVENUE, N.W.  
WASHINGTON, DC 20037

EXAMINER

NICHOLS, CHRISTOPHER J

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 08/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/674,379

Applicant(s)

HONJO ET AL.

Examiner

Christopher Nichols, Ph.D.

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 June 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 9, 14 and 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 10-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-15 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                      | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                             | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>14 19</u> . | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of Group I (claims 1-7 and 11-13) drawn to substantially purified polypeptide, a cDNA encoding said polypeptide, vectors, host cells, and pharmaceutical compositions comprising said polypeptide, and a screening method using said polypeptide in Paper No. 17 (5 June 2003) is acknowledged. Applicant's request to include claims 8 and 10 in Group I is hereby granted.
2. Claims 9 and 14-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7 (5 June 2003).

### *Status of Application, Amendments, and/or Claims*

3. The Preliminary Amendments filed 30 October 2002 (Paper No. 3), Paper No. 4 (10 December 2001), and 5 June 2003 (Paper No. 18) have been entered in full. The Specification has been amended accordingly, claims 14-15 have been added, and claims 1, 2, 4, 5, 6, 8, 10, 11, 12, and 13 have been amended.
4. Claims 1-8 and 10-13 are currently under examination.
5. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Art Unit: 1647

***Specification***

6. The disclosure is objected to because of the following informalities: the first sentence of the specification does not end in a period. Appropriate correction is required.

7. The abstract of the disclosure is objected to because "polypeptid" is misspelled.

Correction is required. See MPEP § 608.01(b).

***Provisional Obvious-Type Non-Statutory Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-8 and 10-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, and 7 of copending Application No. 09/083002 (herein cited as US Patent Application Publication US 2001/0016650 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and Application No. 09/083002 are drawn to polynucleotides and polypeptides that share 100% sequence homology, namely SEQ ID NO: 11, 13, 14, and 15.

Art Unit: 1647

9. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1-8 and 10-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, and 7 of copending Application No. 10/041016 (herein cited as US Patent Application Publication US 2002/0165151 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and Application No. 09/083002 are drawn to polynucleotides and polypeptides that share 100% sequence homology, namely SEQ ID NO: 11, 13, 14, and 15.

11. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a substantially purified form of a polypeptide, said polypeptide comprising the amino acid sequences shown in SEQ ID NO: 13 or 14, cDNA's encoding said polypeptides comprising SEQ ID NO: 11, 12, and 15, host cells, and vectors comprising same,*

Art Unit: 1647

*method of recombinant production of said polypeptides, does not reasonably provide enablement for homologues, fragments, homologues of said fragments of SEQ ID NO: 13 or SEQ ID NO: 14, a fragment cDNA that selectively hybridizes to SEQ ID NO: 11, 12, or 15, or methods of production of fragments, homologues, and homologues of fragments.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

13. The claims are drawn very broadly to fragments, homologues, and homologues of fragments of SEQ ID NO: 13 and 14, as well as fragments of hybridizing polynucleotides which bind SEQ ID NO: 11, 12, and 15. The language of said claims encompasses all fragments, from a single amino acid to a full-length polypeptide minus a single residue.

14. The specification teaches that SEQ ID NO: 11, 12, and 15 encode SEQ ID NO: 13 and

14. A preparation comprising SEQ ID NO: 14 has activity as an inhibitor of aortic vascular smooth muscle proliferation *in vitro* (Figure 2).

15. Yet, the specification fails to provide any guidance for the successful cloning and expression of fragments, homologues, and homologues of fragments of the claimed SEQ ID NO's, and since resolution of the various complications in regards to protein mutagenesis is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of formulations of fragments, homologues, and homologues of fragments of the claimed SEQ ID NO's with full-length SEQ ID NO: 14. In the absence of any guidance from the specification, the

Art Unit: 1647

amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

16. Since the specification as filed does not provide any guidance or examples that would enable a skilled artisan to make or use fragments, homologues, and homologues of fragments of the claimed SEQ ID NO's. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a fragment, homologue, or homologue of a fragment based solely on the performance of a full-length polypeptide is highly problematic. Thus, although the specification prophetically considers and discloses general methodologies of using the claimed fragments, homologues, and homologues of fragments of the claimed SEQ ID NO's, such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

17. The following references are cited herein to illustrate the state of the art of protein biochemistry.

18. Nakamura *et al.* (6 August 1999) "DANCE, a Novel Secreted RGD Protein Expressed in Developing, Atherosclerotic, and Balloon-injured Arteries." The Journal of Biological Chemistry **274**(32): 22476-22483 teaches a polypeptide that shares 100% sequence homology with SEQ ID

Art Unit: 1647

NO: 13 and 14, and a cDNA that shares 100% sequence homology with SEQ ID NO: 11 and 15

(Figure 1). The novel polypeptide discussed by Nakamura et al. is called DANCE:

developmental arteries and neural crest epidermal growth factor (EGF)-like and it is shown to mediate adhesion of endothelial cells through binding to integrins (Figure 10). Thus while establishing a function for the claimed proteins, the reference does not teach what fragments, homologues, or fragments of homologues retain DANCE activity or what the therapeutic effects of DANCE would be as there are not examples provided in the instant specification.

19. Regarding derivatives and fragments of SEQ ID NO: 13 and 14 polypeptides, as well as the cDNA's which encode them, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited.

Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of



Art Unit: 1647

ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research 10:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. 18(1): 34-39, especially p. 36 at Box 2; Doerks *et al.*, (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics 14(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology 15:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics 15(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics 12(10): 425-427]. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification

Art Unit: 1647

regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

20. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from experiments using full-length polypeptides and cDNA to the fragments, homologues, and fragments of homologues as exemplified in the references herein.

21. Claim s **10**, **11**, and **12** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

22. The claims are drawn very broadly to pharmaceutical compositions comprising a polypeptide according to claim 1 or 2. As noted above, claims 1 and 2 are note enabled for the homologues, fragments, or homologues of the fragments as discussed above. The language of said claims encompasses both *in vivo* and *in vitro* uses.

Art Unit: 1647

23. The specification teaches that SEQ ID NO: 11, 12, and 15 encode SEQ ID NO: 13 and 14. A preparation comprising SEQ ID NO: 14 has activity as an inhibitor of aortic vascular smooth muscle proliferation *in vitro* (Figure 2).

24. While sufficient guidance is given regarding performing an *in vitro* screening method, the instant specification fails to provide any guidance for the successful use of an *in vivo* model, especially as a therapeutic agent, and since resolution of the various complications in regards to targeting the role a particular gene in an organism is highly unpredictable, especially concerning diseases and disorders, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination first of a disease or disorder in which SEQ ID NO: 13 and/or 14 was involved and then manifestations of signs and symptoms that correlate with SEQ ID NO: 13 and 14 activity or levels, whether present or absent, less than or greater than normal, or some abnormal form (i.e. mutation of some kind as of yet unspecified). In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

25. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a specific polypeptide *in vivo* activity based solely on its performance *in vitro* is highly problematic (see MPEP 2164.02). Thus, although the specification prophetically considers and discloses general methodologies of using the claimed methods in *in vivo* therapeutic regimens, such a disclosure would not be considered enabling since the state of therapeutic proteins is

Art Unit: 1647

highly unpredictable. The factors listed below have been considered in the analysis of enablement:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

26. The following references are cited herein to illustrate the state of the art of protein biochemistry.

27. Concerning the breadth of the claims and the nature of the invention as a therapeutic, as noted above, no examples of diseases, disorders, injuries, or other maladies are provided by the instant Specification as filed or the prior art as to what the conditions SEQ ID NO: 13 and/or 14 would be useful for treating. While putting forth the proposition of using SEQ ID NO: 13 and/or 14 for treating abnormal growth of a smooth muscle cell, arteriosclerosis, restenosis after PTCA or myosarcoma, no evidence is present in the instant Specification or the prior art as to guide the skilled artisan to use either SEQ ID NO: 13 or 14 as a therapeutic. What remains is an invitation to experiment, first to determine whether SEQ ID NO: 13 or 14 are involved the aforementioned disorders, then determine their role in said disorders, and finally the course of therapy that would have a salubrious outcome {see MPEP §2164.01(a)}. Thus in the absence of guidance and working examples, the skilled artisan is confronted with an undue burden of experimentation in

Art Unit: 1647

an unpredictable and undeveloped art to practice the invention as claimed (in the instant case the role of SEQ ID NO: 13 and 14 in the aforementioned conditions).

28. Nakamura *et al.* (6 August 1999) "DANCE, a Novel Secreted RGD Protein Expressed in Developing, Atherosclerotic, and Balloon-injured Arteries." The Journal of Biological Chemistry **274**(32): 22476-22483 teaches a polypeptide that shares 100% sequence homology with SEQ ID NO: 13 and 14, and a cDNA that shares 100% sequence homology with SEQ ID NO: 11 and 15 (Figure 1). The novel polypeptide discussed by Nakamura *et al.* is called DANCE:

developmental arteries and neural crest epidermal growth factor (EGF)-like and it is shown to mediate adhesion of endothelial cells through binding to integrins (Figure 10). Thus while establishing a function for the claimed proteins, the reference does not teach what fragments, homologues, or fragments of homologues retain DANCE activity. In addition, while an *in vitro* activity assay is demonstrated, no *in vivo* examples are provided.

29. Regarding derivatives and fragments of SEQ ID NO: 13 and 14 polypeptides, see discussion above.

30. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from *in vitro* experiments to the *in vivo* therapeutic method as exemplified in the references herein.

31. Claims 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *an in vitro screening method for an antagonist or agonist SEQ ID NO: 13 or 14*, does not reasonably provide enablement for an in vivo screening method for an antagonist or agonist SEQ ID NO: 13 or 14 or the use of homologues, fragments, homologues of

Art Unit: 1647

*said fragments of SEQ ID NO: 13 or SEQ ID NO: 14.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

32. The claims are drawn very broadly to methods screening for test compounds which affect cell growth. The language of said claims encompasses both *in vivo* and *in vitro* assays.

33. The specification teaches that SEQ ID NO: 11, 12, and 15 encode SEQ ID NO: 13 and 14. A preparation comprising SEQ ID NO: 14 has activity as an inhibitor of aortic vascular smooth muscle proliferation *in vitro* (Figure 2).

34. While sufficient guidance is given regarding performing an *in vitro* screening method, the instant specification fails to provide any guidance for the successful use of an *in vivo* model, and since resolution of the various complications in regards to targeting the role a particular gene in an organism is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination of formulations of signs and symptoms that correlate with SEQ ID NO: 13 and 14 activity or levels. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

35. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a specific polypeptide *in vivo* activity based solely on its performance *in vitro* is highly problematic (see MPEP 2164.02). Thus, although the specification prophetically considers and

Art Unit: 1647

discloses general methodologies of using the claimed methods in *in vivo* assays, such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

36. The following references are cited herein to illustrate the state of the art of protein biochemistry.

37. Nakamura *et al.* (6 August 1999) "DANCE, a Novel Secreted RGD Protein Expressed in Developing, Atherosclerotic, and Balloon-injured Arteries." The Journal of Biological Chemistry 274(32): 22476-22483 teaches a polypeptide that shares 100% sequence homology with SEQ ID NO: 13 and 14, and a cDNA that shares 100% sequence homology with SEQ ID NO: 11 and 15 (Figure 1). The novel polypeptide discussed by Nakamura et al. is called DANCE: developmental arteries and neural crest epidermal growth factor (EGF)-like and it is shown to mediate adhesion of endothelial cells through binding to integrins (Figure 10). Thus while establishing a function for the claimed proteins, the reference does not teach what fragments, homologues, or fragments of homologues retain DANCE activity. In addition, while an *in vitro* activity assay is demonstrated, no *in vivo* examples are provided.

Art Unit: 1647

38. Regarding derivatives and fragments of SEQ ID NO: 13 and 14 polypeptides, see discussion above.

39. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from *in vitro* experiments to the *in vivo* screening methods as exemplified in the references herein.

40. Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

41. The terms "selectively hybridizes" in claims 4 and 5 is a relative term which renders the claim indefinite. The terms "selectively hybridizes" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Neither the specification nor the art defines the term unambiguously. Thus the metes and bounds of the claims cannot be determined.

42. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps by which it is determined whether a given test compound is an agonist or antagonist.



***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

43. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5782234 (16 February 1999) Bandmann *et al.* US 5782234 teaches polypeptides that share 100% sequence homology with SEQ ID NO: 13 and 14 thus meeting the limitations of claims 1 and 2 ("SEQUENCE LISTING"; known as "ECMP"s). US 5782234 teaches cDNA's that share 100% sequence homology with SEQ ID NO: 11 and 15, as well as expression vectors containing said sequences, and host cells transformed with said expression vectors containing said cDNA's thus meeting the limitations of claims 3, 4, 6, 7, and 8 ("SEQUENCE LISTING"; Col. 14-19; claims 1-7). It is of note that US 5782234 does disclose a nucleic acid sequence which shares 99.8% sequence homology to SEQ ID NO: 12, said sequence also shares 100% sequence homology with bp 3-2328 of SEQ ID NO: 12 thus meeting the limitations of claims 1 and 5 (for it includes cDNA's that encode the polypeptides of claim 1). US 5782234 teaches pharmaceutical compositions of said polypeptides thus meeting the limitations of claims 10-12 ("SEQUENCE LISTING"; Col. 24-26). The recitation in the claims of the limitation "pharmaceutical composition" is interpreted as an intended use and is not given patentable weight in this art rejection. Also, the composition of Edwards *et al.* is not inconsistent with such

Art Unit: 1647

treatment. US 5782234 teaches a method of screening for agents which bind ECMP such as agonists thus meeting the limitations of claim 13 (Col. 21 lines 1-20).

*Summary*

44. Claims 1-8 and 10-13 are hereby rejected.

45. The following articles, patents, and published patent applications were found by the Examiner during the prior art search and are here made of note:

a. US Patent Application Publication US 2002/0038006 (28 March 2002) Bandmann *et al.* It is of note because US 2002/0038006 teaches polypeptides that share 100% sequence homology with SEQ ID NO: 13 and 14, cDNA's that share 100% sequence homology with SEQ ID NO: 11 and 15. Further US 2002/0038006 disclose a nucleic acid sequence which shares 99.8% sequence homology to SEQ ID NO: 12, said sequence sharing 100% sequence homology with bp 3-2328 of SEQ ID NO: 12.

b. WO 99/60125 (25 November 1999) Jacobs *et al.* WO 99/60125 teaches polypeptides that share 100% sequence homology with SEQ ID NO: 13 and 14, cDNA's that share 100% sequence homology with SEQ ID NO: 11 and 15. Further US WO 99/60125 disclose a nucleic acid sequence which shares 99.8% sequence homology to SEQ ID NO: 12, said sequence sharing 100% sequence homology with bp 3-2328 of SEQ ID NO: 12.

c. WO 02/07646 A2 (31 January 2002) Flugelrman *et al.* It is of note because WO 02/07646 teaches polypeptides that share 100% sequence homology with SEQ ID NO: 13 and 14, cDNA's that share 100% sequence homology with SEQ ID NO: 11 and 15.

- d. US 2001/0051358 A1 (13 December 2001) Olsen and Li US 2001/0051358 is of note because it teaches polypeptides that share 100% sequence homology with SEQ ID NO: 13 and 14 (Figure 1; claim 10). US 2001/0051358 teaches cDNA's that share 100% sequence homology with SEQ ID NO: 11 and 15, as well as expression vectors containing said sequences, and host cells transformed with said expression vectors containing said cDNA's (Figure 1; paragraphs [0055]-[0076]; claims 1-9).
- e. US 6303765 (16 October 2001) Bandmann *et al.* US 6303765 teaches cDNA's that share 100% sequence homology with SEQ ID NO: 11 and 15, as well as expression vectors containing said sequences, and host cells transformed with said expression vectors containing said cDNA's ("SEQUENCE LISTING"; Col. 14-19; claims 1-10). It is of note that US 6303765 also discloses a nucleic acid sequence which shares 99.8% sequence homology to SEQ ID NO: 12, said sequence also shares 100% sequence homology with bp 3-2328 of SEQ ID NO: 12.

Art Unit: 1647

### **Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*Elizabeth C. Kemmerer*

CJN  
August 4, 2003

**ELIZABETH KEMMERER  
PRIMARY EXAMINER**